REMARKS

The Office Action mailed on June 2, 2009, has been reviewed and the comments of the Examiner carefully considered. Claims 1-6, 11, 13-16, 18, 19 and 22 are pending and currently stand rejected. Claims 1, 11 and 22 have been amended. Claim 2 has been canceled. Support for these amendments may be found in the specification and in canceled claim 2. No new matter is believed to have been added by way of these amendments.

Claim Objections

The Examiner objected to claim 1 for the use of periods after the Roman numerals I, II and III. Applicants have amended claim 1 herein to remove the periods, as recommended by the Examiner.

The Examiner objected to claim 11 for the use of a dash ("-") immediately preceding and immediately following the amino acid sequences listed in the claim. Applicants have amended claim 11 herein to remove the extra dashes, as recommended by the Examiner.

Applicants submit that, in view of the amendments to the claims made herein, the Claim Objections have been overcome.

Objection to the Specification

The Examiner objected to the Specification for inconsistency with respect to the spelling of the name of one of the inventors. Applicants submit herewith an Application Data Sheet, which includes the correct spelling of the name of inventor Derek Silcock. Accordingly, Applicants submit that the Objection to the Specification has been overcome.

Rejections under 35 U.S.C. § 112, Second Paragraph ("Indefiniteness")

The Examiner rejected various claims as allegedly being indefinite for the reasons set forth below.

As a preliminary matter, claim 2 has been cancelled, rendering moot the rejection of this claim.

1. Claims 1-6, 13-16, 18, 19 and 22 were rejected as allegedly indefinite for recitation of the phrase "protease associated with wound fluid". The rejection alleges that there is not

sufficient linkage between this phrase, and the phrases "protease associated with wound infection or ulcer formation". Applicants respectfully disagree. Applicants direct the Examiner's attention to the Detailed Description. At lines 4-8 on page 4 of the specification, "protease associated with wound infection" is defined as including proteases that are elevated during infection and proteases that are elevated in wounds that are apparently not clinically infected but which go on to become infected within a few days. A "protease associated with ulcer formation" is defined as including proteases that are elevated in chronic wounds. Accordingly, each phrase is explicitly defined as used in the present patent application. Further, because both terms are defined, Applicants emphasize that, as the examiner has suggested, that the phrases are not merely synonyms, but rather, that the phrases have distinct meanings, supported by the specification. Furthermore, at lines 16-20 on page 2 of the specification, Applicants describe that it, in part, the invention encompasses a situation in which wound fluid from wounds that are apparently not clinically infected but which go on to become infected within a few days have elevated levels of neutrophil elastase activity and may also have high levels of other inflammatory enzymes, such as macrophage proteases, other neutrophil proteases, bacterial collagenase, plasmin, hyaluronidase, kallikrein or t-PA. In this way, Applicants not only describe the wound fluid, but describe examples of situations in which would fluid would include proteases associated with would infection.

2. Claims 1-6, 13-16, 18, 19 and 22 were also rejected as allegedly indefinite for recitation of the term "associated", as used in the phrase "protease associated with wound fluid". The Examiner argues that the term may indicate proteases in the wound fluid itself, as well as proteases that are produced or upregulated as a result of an infection, and the protease is not necessarily in the wound fluid. Applicants respectfully submit that based on the use of the term in the specification, the term "associated" encompasses both descriptions set forth by the Examiner, and should not be limited to one or the other definition. This broad definition of "associated" is supported throughout the specification, and by the definitions of the phrases described immediately above.

3. Claims 1-6, 13-16, 18, 19 and 22 were also rejected as allegedly indefinite for recitation of the term "apparently not clinically infected." Applicants respectfully submit that the entire specification provides sufficient guidance to define this term, and for example, the text on pages 1 and 2 of the specification describe the signs of infection used in a clinical setting, in

contrast to the aspects of infection not presenting clinically. By way of a further example, a wound that does not demonstrate outward signs of clinical infection (e.g., redness, swelling), but one which is nonetheless infected (such as by an indicator set forth in the present invention), is one example of a wound that is apparently not clinically infected. Applicants submit that the usage of the term is fully supported throughout the specification, and therefore, the term is not indefinite.

4. Claim 3 was rejected for use of the term "other factors". The term "factors" is exemplified on page 4 of the specification as "other proteases" present in the wound fluid, using language which mirrors the claim language. The term "other factors" is also used in context of a factor that can degrade a polymer as set forth in the specification. Accordingly, based on the use of the term in the specification, Applicants respectfully submit that the term is not indefinite.

5. Claim 6 was rejected for recitation of the language "3 to 15" amino acids. Applicants submit that, based on the usage of this phrase in the specification, this phrase should clearly be understood to refer to a peptide of "3 to 15 amino acid residues in length". For example, at lines 4-10 on page 6, it is set forth that "Oligopeptides are generally defined as polypeptides of short length, typically twenty amino acids or fewer. Preferably, the oligopeptidic sequences employed in the present invention consist of 3 to 15 amino acids...". The use of the phrase in this context makes the meaning of the phrase unambiguous.

6. Finally, the term "substantially" was rejected as allegedly being indefinite. Applicants respectfully disagree. The term is used throughout the specification, and is exemplified in multiple instances (e.g., "substantially impervious", "substantially encapsulates"). By way of a non-limiting example, lines 11-19 on page 15 of the specification sets forth that:

> Preferably, the backing layer is substantially liquid-impermeable. The backing sheet is preferably semipermeable. That is to say, the backing sheet is preferably permeable to water vapour, but not permeable to liquid water or wound exudate. Preferably, the backing sheet is also microorganism-impermeable. Suitable continuous conformable backing sheets will preferably have a moisture vapor transmission rate (MVTR) of the backing sheet alone of 300 to 5000 $g/m^2/24$ hrs, preferably 500 to 2000 g/m.sup.2/24 hrs at 37.5° C. at 100% to 10% relative humidity difference. The backing sheet thickness is preferably in the range of 10 to 1000 micrometers, more preferably 100 to 500 micrometers.

In this way, the usage and support of the term substantially makes the substance and scope of the term unambiguous. The term "substantially" is permissible under well-established patent law, when exemplified as in the present application. For example, MPEP § 2173.05(b)(D.) provides that the term "substantially" can be definite in view of general guidelines presented in the patent application. Such is the case with Applicants use of the term in the present application.

Accordingly, because the presently-amended claims are not indefinite, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, First Paragraph ("Written Description")

Claims 1-6, 13-16, 18, 19, and 22 were rejected as allegedly lacking written description. Applicants' best understanding of the Written Description rejection is that the rejection appears to be an assertion that the specification allegedly does not provide adequate written description for the following aspects of the claims: 1.) Proteases in the wound fluid; 2.) Oligopeptides that are cleavable by a protease; 3.) Matrix comprising polymers and a therapeutic agent; 4.) Wound dressings and methods of making such dressings. Applicants respectfully disagree with all of the Written Description rejections set forth in the office action, for the following reasons.

As a preliminary matter, claim 2 has been cancelled, rendering moot the rejection of this claim.

Regarding the proteases in the wound fluid, Applicants submit that the response to the Indefiniteness rejection above applies with equal force in response to the Examiner's Written Description rejection. That is, Applicants have provided examples of wound fluids that may contain proteases that may be associated with wound infection. Nonetheless, in the interest of advancing prosecution of the application, Applicants have canceled claim 2 and amended claim 1 to include the subject matter of claim 2, to recite that the protease in the wound fluid is a protease associated with wound infection or ulcer formation. Furthermore, pages 1-3 of the Specification provide abundant description of proteases associated with wound fluid, as encompassed by the claims.

Regarding oliogpeptides that are cleavable by a protease, Applicants direct the Examiner's attention to page 6 of the specification. Furthermore, pages 8 and 9 of the specification provide abundant description of specific protease sequences cleavable by specific proteases, and provide guidance to the skilled artisan as to the scope of the oligopeptides

encompassed by the claims. The claims are supported by sufficient Written Description, as the oligopeptides encompassed by the claim are well-defined. The oligopeptides are cleavable by a protease associated with wound fluid, wherein the protease is associated with wound infection or ulcer formation. The peptides are further described on page 6 of the specification. Contrary to the assertions in the Office Action, this is indeed a finite group of oligopeptides. As set forth previously, unique cleavage by particular enzyme, isolelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See, e.g.,* Lockwood v. American Airlines, 107 F.3d 1565,1572 (Fed. Cir. 1997). The claimed peptides are described with similar detail, and therefore, are supported by adequate Written Description.

Regarding the rejection of the matrix comprising a therapeutic agent, Applicants respectfully submit that the entire specification, and for example, pages 5 and 6, provides abundant support for a matrix comprising a therapeutic agent. Therefore, Applicants have provided more support that what is required by the corresponding patent laws. As provided in the case of *Falkner v. Inglis* (448 F.3d 1357, 1366 (Fed. Cir. 2006)), explicit examples are not necessary to support the adequacy of Written Description. As set forth previously, the incorporation of a therapeutic agent into a matrix such as those set forth in the present specification is something that is well known in the art. Indeed, MPEP § 2164.05(b) provides that "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." (Citing *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)).

Furthermore, while the Examiner alleges that the present specification does not properly incorporate by reference PCT Publication No. WO00/64486, Applicants submit that this reference need not be incorporated by reference for the purpose of providing "essential material". This reference merely provides one example of the state of art at the time of filing. This reference provides a description of non-essential material, and therefore, is properly incorporated by reference in the present application.

While not in agreement with the Examiner's basis of rejection, Applicants have also amended claims 1 and 22 such that there is at most one backing layer. Support for this amendment is found in the claims themselves, as well as throughout the specification.

Accordingly, because all of the currently pending claims are supported by the required Written Description, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 103(a)

1. Claims 1-4, 6, 13-16, 18, 19 and 22 were rejected as allegedly being obvious over Peppas (Eur. J. Pharmaceutics and Biopharmacetics (2000) 50:27-46) and Suzuki (J. Biomed. Mater. Res. (1998) 42:112-116) and Arnold (EP Patent No. 0599589). The examiner argues that one of skill in the art would be motivated to combine hydrogel wound dressing taught by Pappas with the antibiotic-release wound dressings of Suzuki and the multi-layer wound dressings taught by Arnold. It is the Examiner's view that the combination of the cited patents would lead one of skill in the art to arrive at claims 1-4, 6, 13-16, 18, 19 and 22, in their entirety. Applicants respectfully traverse the Examiner's rejection for the following reasons.

As a preliminary matter, claim 2 has been cancelled, rendering moot the rejection of this claim.

The test which must be met for a reference or a combination of references to establish obviousness has not been satisfied in the instant matter. The MPEP states, in relevant part, the proper test for obviousness:

> Office policy is to follow Graham v. John Deere Co. in the consideration and determination of obviousness under 35 U.S.C. § 103 ...
>
> [T]he four factual inquires enunciated therein as a background for determining obviousness are as follows:
>
> (A) Determining the scope and contents of the prior art;
> (B) Ascertaining the differences between the prior art and the claims in issue;
> (C) Resolving the level of ordinary skill in the pertinent art; and
> (D) Evaluating evidence of secondary considerations. (MPEP § 2141).

When applying 35 U.S.C. § 103, the following tenets of patent law must be followed: 1) the claimed invention must be considered as a whole; 2) the references must be considered as a

whole; 3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and 4) reasonable expectation of success is the standard with which obviousness is determined. MPEP § 2141 II. This test has not been satisfied here for any of the obviousness rejections.

To begin with, Suzuki teaches only the attachment of antibiotic, via chemical crosslinking of peptidyl moities, to a polymeric layer. The references do not provide any teaching or suggestion of the currently claimed pore structure, which releases therapeutic agent as the protease specifically cleaves oligopeptides to increase pore size.

In contrast to what is alleged in the Office Action, the protease "associated" with the wound fluid in the present claims is not overly broad, and therefore, the use of this term as a basis for the obviousness rejection is unfounded. The protease associated with wound fluid, according to the amended claims, is a protease associated with a wound infection and with ulcer formation. None of the cited references teaches this. Furthermore, none of the references teaches or suggests a matrix comprising polymers joined by cross-linkages which cross-linkages comprise oligopeptidic sequences which are cleavable by a protease associated with wound fluid such that the rate of release of the therapeutic agent increases in the presence of the protease. Therefore, there is nothing in any of the cited references or known in the art that would lead the skilled artisan to arrive at the presently-amended claims.

Consequently, because none of the rejected claims are obvious, as set forth above, Applicants respectfully request withdrawal of the rejection of claim 1 under 35 U.S.C. § 103(a). Further, applicants submit that claims 2-4, 6, 13-16, 18, 19 and 22 are thereby allowable as written as depending from an allowable independent claim.

2. Claims 1-4, 6, 13-16, 18, 19 and 22 were rejected as allegedly being obvious over Peppas, Suzuki, and Arnold, further in view of Ulbrich et al. (Journal of Controlled Release 2000, 64:63-70). Applicants respectfully traverse the Examiner's rejection for the following reasons.

As a preliminary matter, claim 2 has been cancelled, rendering moot the rejection of this claim.

The Office Action states that the teaching of N-(2-hydroxypropyl)methacrylamide (HPMA) by Ulbrich further makes the claimed invention obvious to one of skill in the art. Applicants submit that Ulbrich's teaching in no way makes up for the deficiencies of Peppas,

Suzuki, and Arnold, as set forth above, and therefore, that nothing about the combination of Peppas, Suzuki, Arnold, and Ulbrich would make the amended claims obvious, because Ulbrich does not provide any teaching or suggestion that the protease associated with wound fluid, according to the amended claims, is a protease associated with a wound infection and with ulcer formation, and furthermore, Ulbrich does not provide any teaching or suggestion that a matrix comprising polymers joined by cross-linkages which cross-linkages comprise oligopeptidic sequences which are cleavable by a protease associated with wound fluid such that the rate of release of the therapeutic agent increases in the presence of the protease. Therefore, there is nothing in any of the cited references or known in the art that would lead the skilled artisan to arrive at the presently-amended claims.

Consequently, because none of the rejected claims are obvious in view of Peppas, Suzuki, Arnold, and Ulbrich, as set forth above, Applicants respectfully request withdrawal of the rejection of claim 1 under 35 U.S.C. § 103(a). Further, applicants submit that claims 2-4, 6, 13-16, 18, 19 and 22 are thereby allowable as written as depending from an allowable independent claim.

3. Claims 1-6, 11, 13-16, 18, 19 and 22 were rejected based on a combination of Peppas, Suzuki, Arnold, and Ulbrich, further in view of Pachence (WO00/64486). Applicants respectfully traverse the Examiner's rejection for the following reasons.

As a preliminary matter, claim 2 has been cancelled, rendering moot the rejection of this claim.

The Office Action states that the teaching of peptide linkers by Pachence further makes the claimed invention obvious to one of skill in the art. Applicants submit that Pachence's teaching in no way makes up for the existing deficiencies of Peppas, Suzuki, Arnold, and Ulbrich as set forth above, and therefore, that nothing about the combination of Peppas, Suzuki, Arnold, Ulbrich, and Pachence would make the amended claims obvious, because Pachence does not provide any teaching or suggestion that the protease associated with wound fluid, according to the amended claims, is a protease associated with a wound infection and with ulcer formation, and furthermore, Pachence does not provide any teaching or suggestion that a matrix comprising polymers joined by cross-linkages which cross-linkages comprise oligopeptidic sequences which are cleavable by a protease associated with wound fluid such that the rate of release of the therapeutic agent increases in the presence of the protease. Therefore, there is nothing in any of

the cited references or known in the art that would lead the skilled artisan to arrive at the presently-amended claims.

Consequently, because none of the rejected claims are obvious in view of Peppas, Suzuki, Arnold, Ulbrich, and Pachence as set forth above, Applicants respectfully request withdrawal of the rejection of claim 1 under 35 U.S.C. § 103(a). Further, applicants submit that claims 2-4, 6, 13-16, 18, 19 and 22 are thereby allowable as written as depending from an allowable independent claim.

Double Patenting Rejection

Claims 1-6, 11, 13-16, 18, 19 and 22 were rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-4 and 7-16 of copending Application No. 12/041,955 in view of Arnold. Applicants disagree with the grounds for rejection. However, at this time, Applicants respectfully request that the double patenting rejection be held in abeyance until claims in either this or the copending application are deemed to be allowable. At the time claims from one of the applications are found to be allowable, Applicants will consider the Examiner's rejection in view the final version of the allowable claims.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 963-5809 to clarify any unresolved issues raised by this response.

The Director is hereby authorized to charge/credit Deposit Account No. **50-0310** (Billing No. 101713-5030) for any other required fees, deficiencies or overpayments in connection with this Response.

Respectfully submitted,

DEREK SILCOCK ET AL.

Date: October 2, 2009

By: _____

Thomas M. Sossong, Jr., Ph.D.
Registration No. **48,463**
MORGAN, LEWIS & BOCKIUS LLP
1701 Market Street
Philadelphia, PA 19103-2921
Telephone: (215) 963-5809
Facsimile: (215) 963-5001
E-Mail: tsossong@morganlewis.com